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Abstract

Photodynamic therapy (PDT) is an attractive cancer treatment. Talaporfin sodium, a second-generation photosensitizer, results in lower systemic toxicity and relatively better selective tumor destruction than first-generation photosensitizers. However, the mechanism through which PDT induces vascular shutdown is unclear. In this study, the in vitro effects of talaporfin sodium-based PDT on human umbilical vein endothelial cells (HUVECs) were determined through cell viability and endothelial tube formation assays, and evaluation of the tubulin and F-actin dynamics and myosin light chain (MLC) phosphorylation. Additionally, the effects on tumor blood flow and tumor vessel destruction were assessed in vivo. In the HUVECs, talaporfin sodium-based PDT induced endothelial tube destruction and microtubule depolymerization, triggering the formation of F-actin stress fibers and a significant increase in MLC phosphorylation. However, pretreatment with the Rho-associated protein kinase (ROCK) inhibitor, Y27632, completely prevented PDT-induced stress fiber formation and MLC phosphorylation. The in vivo analysis and pathological examination revealed that the PDT had significantly decreased the tumor blood flow and the active area of the tumor vessel. We concluded that talaporfin sodium-based PDT induces the shutdown of existing tumor vessels via the RhoA/ROCK pathway by activating the Rho-GTP pathway and decreasing the tumor blood flow.